REMARKS

Reconsideration and allowance of the present application based on the above amendments and the following remarks are respectfully requested.

By the above amendments, Claims 47 and 48 have been cancelled and Claims 44, 49, 51 and 52 have been amended to remove certain informalities pointed out in the Official Action. As well, the specification has been amended to include an indication of the priority claimed by the subject application.

The objection to the specification for possible spelling errors and incorrect trademark recitations is noted. Corrections of those errors will be provided in due course.

In the Official Action, Claims 44-55 were rejected under 35c U.S.C. §112, first paragraph, for alleged lack of written description of the claimed invention. This rejection is respectfully traversed for at least the following reasons.

In the Official Action, it is alleged that the specification as originally filed does not provide support for the recitation "wherein prolonged humoral immune suppression means that antibody production remains suppressed after the anti-gp39 antibody has been cleared from the subject." Applicants respectfully disagree. The specification as originally filed provides ample support for the prolonged humoral suppression as presently claimed. For example, the specification at page 12, last paragraph, defines "prolonged suppression" to mean that suppression of the antibody production against a TD antigen is maintained after administration of a gp39 antagonist *in vivo* has been terminated. In addition, as discussed for example in the first paragraph of page 25, the half life of anti-gp39 is about 12 days. Moreover, as described in Figure 6B, anti-gp39 is essentially cleared by 21 days after the administration of the antibody. Figure 1B and the discussion thereof in the paragraph bridging pages 20 and 21, shows that a prolonged inhibition is maintained 19 days after

administration of the antibody. Thus, based on the specification, particularly the drawings and the discussion thereof provided in the specification, there is ample written description for the prolonged humoral suppression as presently claimed. Accordingly, the rejection under the first paragraph of §112 is improper and should be withdrawn.

Claims 44-55 were rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness. This rejection is respectfully traversed for at least the following reasons.

The claims were objected to for not defining the term "TD," at least at the first occurrence of the term. Claim 44 has been revised to recite the term "thymus dependent." Thus the objection has been rendered moot and withdrawal thereof is respectfully requested.

As well, the claims have been revised to delete antagonists other than anti-gp39 antibody. Thus the objection under the second paragraph of §112 to the recitation "wherein prolonged humoral suppression means that antibody production remains suppressed after the anti-gp39 antibody has been cleared from the subject" has been obviated and withdrawal thereof is respectfully requested.

In view of the foregoing it is believed that the claims now under consideration fulfill the requirements of the first and second paragraphs of section 112 of the Patent Statute.

In the Official Action, Claims 51-53 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cobbold et al. (U.S. Patent No. 6,056,956) in view of Lederman et al. (U.S. Patent No. 5,474,771) or Armitage et al. (U.S. Patent No. 6,087,329). Claims 50, 54 and 55 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cobbold et al. in view of Lederman et al. or Armitage et al. and in view of Ramanathan et al. (WO 91/09059). These rejections are respectfully traversed for at least the following reasons.

As noted above, the presently claimed invention is directed to prolonged humoral immunity suppression to an administered TD antigen, e.g., a therapeutic antibody. Specifically, the prolonged humoral immunity suppression according to the invention is such that antibody production remains suppressed after the anti-gp39 antibody has been cleared from the subject.

The documents relied upon in the Official Action fail to suggest the claimed invention. In particular, the documents relied upon in the Official Action fail to suggest co-administration of a TD antigen and an anti-gp39 antibody. Moreover, the documents relied upon in the Official Action fail to appreciate that prolonged suppression of humoral immunity will be achieved through the claimed coadminstration.

At the outset, it is noted that while the Official Action acknowledges that Cobbold et al is directed to CD4-specific antibodies and not to gp39 antibodies. Nothing in the Official Action supports equating the effects of a CD4 antibody and a gp39 antibody.

Moreover, contrary to the Office Action, Applicants respectfully submit that the prior art, at best, would only suggest the global suppression of a humoral immune response to antigens for a transient period of time. That is to say, the prior art arguably would suggest suppressing the production of antibodies to an array of antigens to which a particular host is being exposed for a transient, short period of time.

However, it could not have been reasonably predicted that humoral immune responses could be selectively suppressed for prolonged periods of time to desired antigens, i.e., in an antigen-specific manner by the administration of a an anti-gp39 antibody proximate to the time the host becomes exposed to the particular antigen.

More specifically, it could not have been reasonably predicted prior to the present invention that humoral immunity would be suppressed to specific antigens for long period of

time, i.e., even after the anti-gp39 antibody has been cleared from the subject. To the contrary, at best, the reasonable expectation, based on what had been reported, would have been that antibody responses could be suppressed globally for short periods of time while the anti-gp39 antibody remains in the system of a treated subject. However, it could not have been reasonably expected that humoral immune responses to a specific antigen would remain suppressed even after administration of the gp39 antagonist was discontinued and the anti-gp39 antibody was cleared from the subject. The fact that prolonged antigen-specific humoral immune suppression is achieved, and support for such claims, may be found at page 12, last paragraph, of the disclosure, and the Examples. Note, e.g., Example 2, wherein it is reported that humoral immune responses to a TD antigen (KLH) remained suppressed for at least 14 days after treatment.

Therefore, surprisingly, the present invention provides an effective target for prolonged therapeutic manipulation of humoral immune responses to desired antigens. A significant therapeutic application of the invention is to eliminate or suppress humoral immune responses to desired TD antigens, e.g., therapeutic antibodies or recombinant viral vectors, for prolonged periods of time. This is particularly advantageous in the context of therapeutics that must be administered chronically, that may elicit a humoral immune response. This is disadvantageous as it may result in the neutralization of the therapeutic activity thereof.

Thus, there is no *prima facie* case of obviousness against the present claims based on Cobbold et al., taken alone or in combination with the secondary references. Accordingly, the 103 rejections should be withdrawn and such favorable action is respectfully requested.

In the Official Action, Claims 44-55 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 1-17 of

U.S. Patent No. 5,942,229. It is respectfully requested that this rejection be stayed in abeyance until the subject application is otherwise in condition for allowance. At such time, Applicants will file a Terminal Disclaimer if appropriate.

Based on the foregoing, this application is believed to be in condition for allowance. A Notice to that effect is earnestly solicited.

However, if any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so that prosecution may be expedited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached Appendix is captioned **"Version with markings to show changes made"**.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification has been amended to insert the following paragraph in page 1, before line 1:

-- The present application is a divisional application of Serial No. 08/475, 873, filed June 7, 1995, now U.S. Patent No. 5,942,229, which is a continuation of Application Serial No. 08/115,990 filed September 2, 1993. The present application also claims priority to International Application No. PCT/US94/09872, filed September 2, 1994.--

IN THE CLAIMS:

Claims 47 and 48 has been cancelled.

Please amend the following claims:

44. (Amended) A method for inducing prolonged humoral suppression in a subject in need of such prolonged humoral immune suppression to a soluble [TD] thymus dependent (TD) antigen which method comprises:

(i) administering a soluble TD antigen to which a humoral immune reaction is to be suppressed; and

(ii) administering an amount of [gp39 (CD40 ligand) antagonist selected from the group consisting of] an anti-gp39 antibody[,] or a fragment thereof that binds gp39, [soluble CD40, soluble CD40 fusion,] in an amount effective to provide for prolonged humoral immune suppression to said soluble TD antigen, wherein prolonged humoral immune suppression means that antibody production remains suppressed after the anti-gp39 antibody has been cleared from the subject.

49. (Amended) The method of Claim [47] 44, wherein said anti-gp39 antibody is an anti-human gp39 antibody.

51. (Amended) The method of Claim [47] 44, wherein the anti-gp39 antibody is a humanized antibody.

52. (Amended) The method of Claim [47] 44, wherein the antibody comprises human constant regions and non-human variable regions.

END OF APPENDIX